Wyeth

To: Dockets Management Branch (HFA-305) **Date:** October 17, 2003
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852
Docket No. 03N-0016

Subject: Docket No, 2003D-0412: Comments on September 15, 2003 Federal Register: International Conference on Harmonization; Draft Guidance on E2D Postapproval Safety Data Management; Definitions and Standards for Expedited Reporting. 68 Fed.Reg. 53983.

Dear Sir/Madam:

Wyeth respectfully submits these comments on the International Conference on Harmonization (ICH) E2D draft guidance on post approval definitions and standards for expedited reporting. Wyeth is one of the world's largest research-based pharmaceutical and healthcare products companies, and is a leading developer, manufacturer and marketer of prescription drugs, biological products and over-the-counter medications. As such, Wyeth is strongly supportive of any initiatives to harmonize worldwide safety reporting standards and definitions.

Wyeth supports the standards and definitions set forth in the draft ICH E2D guidance. Wyeth encourages FDA not only to adopt the draft guidance, but also to consider the definitions and standards set forth in the ICH E2D draft guidance in the process of revising its proposed rule, Safety Reporting Requirements for Human Drug and Biological Products, to incorporate public comments. 68 Fed.Reg. 12406 (March 14, 2003). Since FDA is in the process of revising its safety reporting regulations including introducing new definitions, FDA is in an excellent position to further worldwide harmonization by adopting the definitions and standards in ICH E2D as part of these regulatory revisions.

Wyeth also has the following comments on the text of the draft guidance:

1. Section 2.5.1.2 (lines 214-16). The draft guidance states that companies are responsible for regularly screening worldwide literature for reporting purposes. The guidance also states that company offices are encouraged to be aware of publications in local journals and bring them to the attention of company safety departments. Wyeth suggests that the guidance clarify that company offices are only responsible for reviewing

local literature for safety reporting purposes if that literature is not already a part of a company's systematic worldwide literature search process. This clarification will help companies avoid the possibility of submitting duplicate reports.

2. Section 2.5.1.2 (lines 211-12 and lines 351-55). The guidance clarifies that an individual case safety report (ICSR) should be submitted for each individual patient identified in a literature article. At section 4.1 discussing identifiable patients, the guidance clarifies that in the absence of a qualifying descriptor (such as gender), a report referring to a definite number of patients ("two patients experienced...") should not be regarded as a case until patient identifiable information is obtained via follow-up. Wyeth is supportive of this definition of an identifiable patient. Wyeth suggests the Agency clarify that this requirement for an identifiable patient applies to literature reports. That is, as section 4.1 is written, a literature article stating "four patients experienced X event," would not qualify as an ICSR unless the article contained other information describing the patients.

3. Section 2.5.2 (lines 240-49). Wyeth supports treating information from solicited sources as study reports. However, for solicited sources such as registries, surveys and disease management programs, causality assessments are not often available. In the case of studies, a causality of "unknown" is usually treated, for reporting purposes, as related and companies follow-up to obtain a causality assessment from the investigator. Please clarify the expectation for reporting unknown causality for other solicited sources; Wyeth suggests treating these solicited cases as unrelated until medical confirmation of association with a drug product is received.

4. Section 3.1.2 (lines 287-89). Please clarify or provide examples of the Agency's expectation of "promptly" communicating "other observations that could change the risk-benefit evaluation" for a product. It is unclear whether the type of report or the types of data that ICH was contemplating should be submitted under this section. Companies are already required to notify regulatory authorities of changes to a product's risk profile via labeling changes. Wyeth suggests that the labeling process is the appropriate mechanism for notifying agencies of this type of information.

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5. Section 3.1.2.1 (lines 292-98). Please provide additional guidance or examples of where expedited reporting should be "considered" for reports of lack of effect for products used to treat life-threatening diseases. That is, some products are used to treat diseases that may be, in their most severe form, life threatening but are not life threatening in every instance (ie, products used to treat both arrhythmias and myocardial infarction). Wyeth suggests that events of lack of effect with these types of products should only be reported on an expedited basis if the event is actually life threatening and hence meets the definition of serious. If the lack of effect does not result in a life threatening adverse event, the ICSR should not be expedited.

6. Section 4.4 (lines 400-30). The guidance states that companies are encouraged to actively query the reporter to elicit the most complete account of an event possible. The guidance states that telephone calls, site visits and letters should be used as needed to optimize the chances to obtain follow-up information. In addition, the guidance encourages companies to use targeted questionnaires to obtain follow-up information. The guidance also prioritizes types of cases and data elements that should be sought via follow-up. Wyeth strongly encourages FDA to consider adopting this flexible approach, rather than the more rigid approach described in the Proposed Rule, thus allowing companies to tailor follow-up methods to achieve the best results.

We hope the Agency finds these comments useful.

Sincerely,

Wendy P. Stephenson

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